L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2002:695722 CAPLUS
TI Methods for treating genetically-defined proliferative disorders characterized by a non-random chromosomal aberration with heat shock protein HSP90 inhibitors
IN Fritz, Lawrence C.; Burrows, Francis J.
PA Conforma Therapeutics Corp., USA
SO PCT Int. Appl., 390 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069900	A2	20020912	WO 2002-US6518	20020301

PI
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-272751P P 20010301

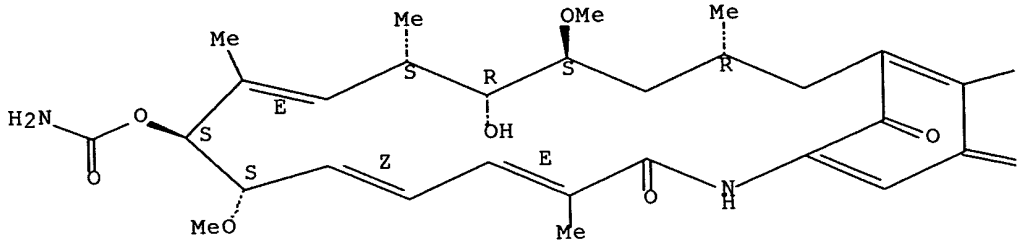
AB Applicants report that many proliferative disorders are assocd. with aberrant proteins that exhibit a dependence on HSP90. In some cases this dependence manifests as a heightened sensitivity to HSP90 inhibitors such that affected cells can be selectively treated using a dosage that is effective against the aberrant cells but which is ineffective or less effective against normal cells. The aberrant proteins may also exhibit increased proteasome-dependent degrdn. when in the presence of HSP90 inhibitors. While the invention is not limited by mechanism, increased dependence, sensitivity, and /or disposition to preferential degrdn. may advantageously be used to treat corresponding proliferative diseases according to the methods of the invention. The invention relates generally to methods of treating cell proliferative diseases with HSP90 inhibitors and, depending on the specific aspect and embodiment(s) claimed, to the treatment of proliferative diseases that are assocd. with fusion proteins, e.g., bcr/abl, or mutant proteins or cellular protein isoforms, e.g., mutant forms of p53.

IT **459174-35-7P 459174-38-0P 459174-42-6P**
459174-45-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods for treating genetically-defined proliferative disorders characterized by non-random chromosomal aberration with heat shock protein HSP90 inhibitors)

RN 459174-35-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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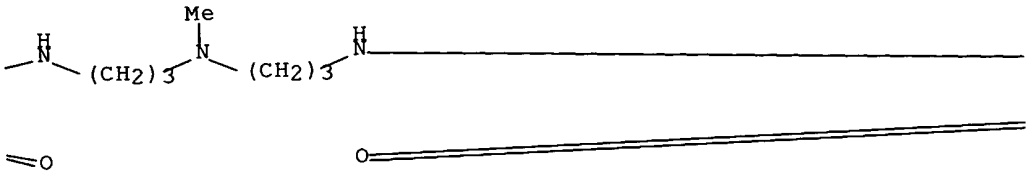

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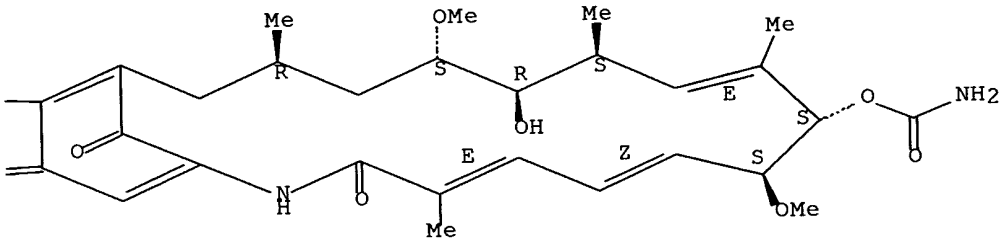
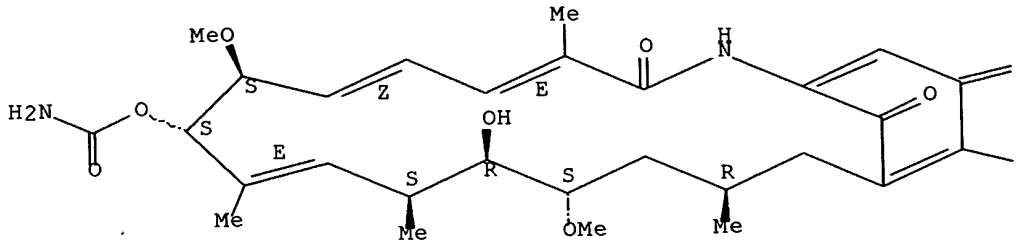


RN 459174-38-0 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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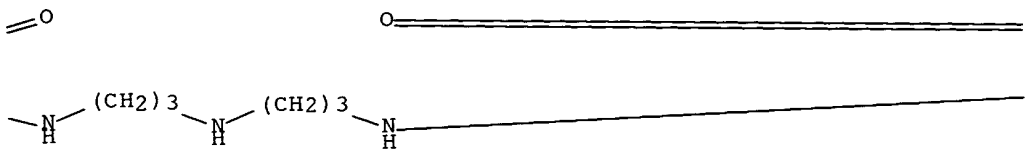

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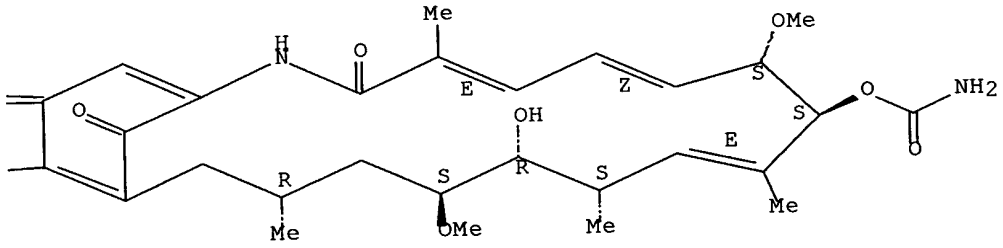

RN 459174-42-6 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.
Double bond geometry as described by E or Z.

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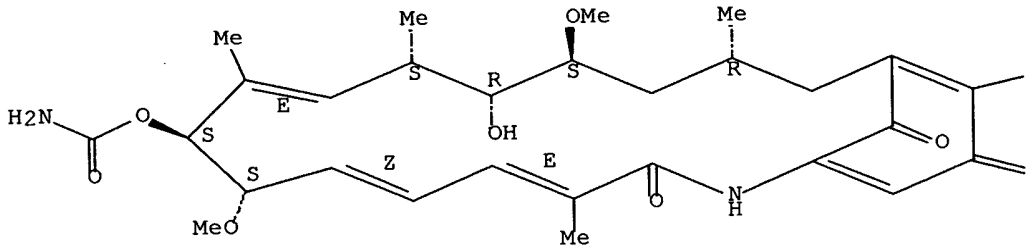

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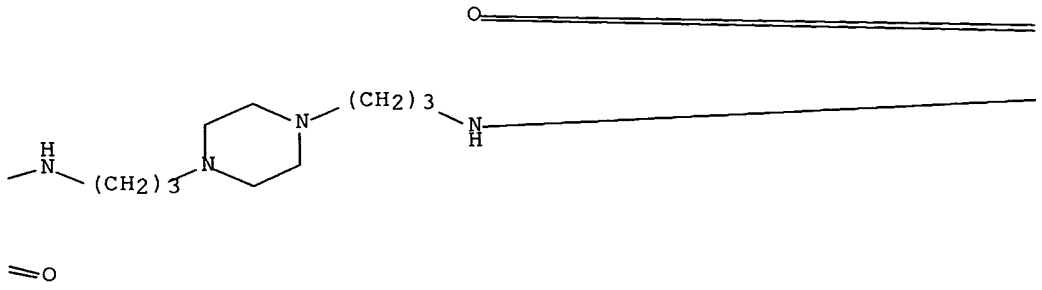

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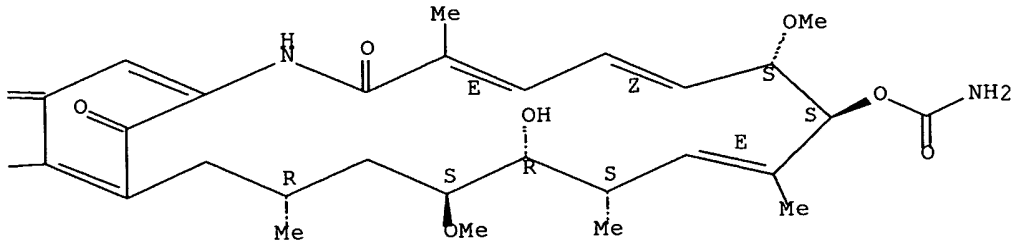
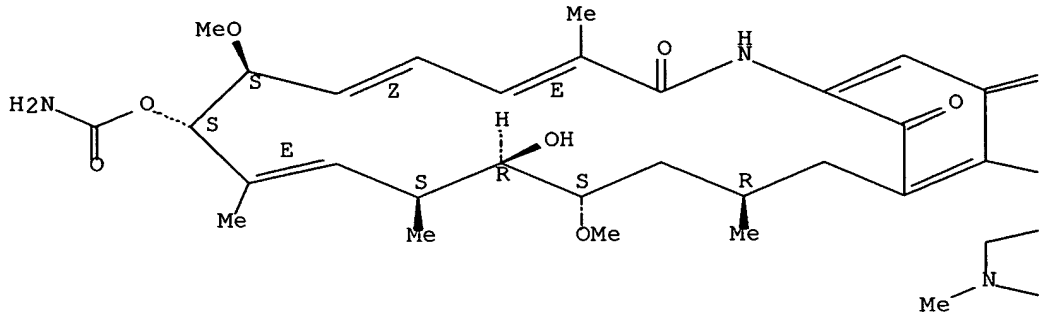


RN 459174-45-9 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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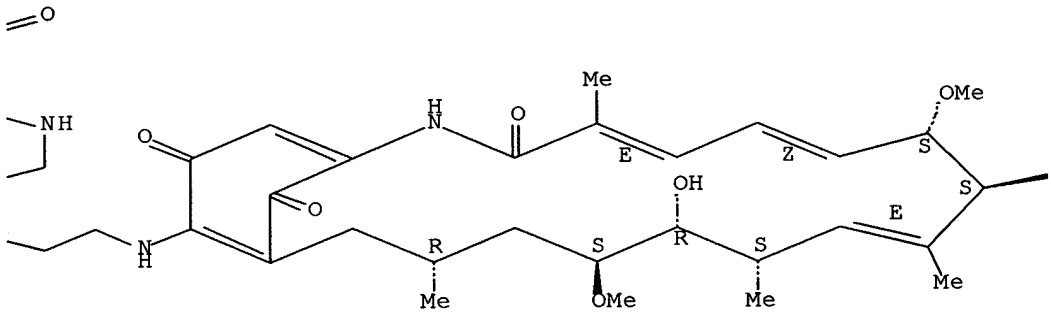

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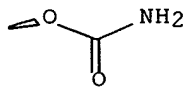

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2000:742091 CAPLUS
DN 133:305587
TI Methods and compositions using bifunctional hsp-binding derivatives for degradation and/or inhibition of HER-family tyrosine kinases and treatment of cancer
IN Rosen, Neal; Kuduk, Scott D.; Danishefsky, Samuel J.; Zheng, Furzhong F.; Sepp-Lorenzino, Laura; Ouerfelli, Ouathek
PA Sloan-Kettering Institute for Cancer Research, USA
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1169319	A1	20020109	EP 2000-921985	20000407
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 2002045570	A1	20020418	US 2001-960665	20010921
PRAI	US 1999-128593P	P	19990409		
	WO 2000-US9512	W	20000407		

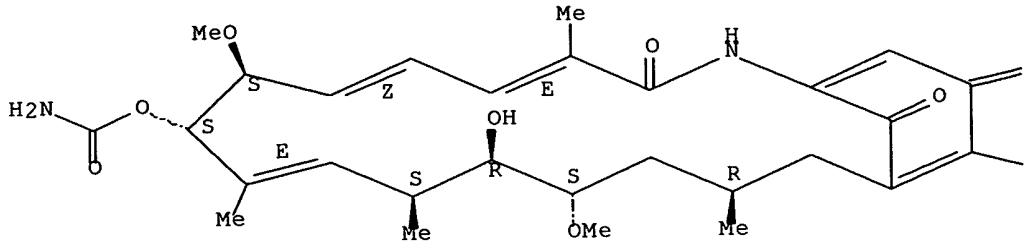
AB Bifunctional mols. comprising two hsp-binding moieties which bind to hsp90 in the pocket to which ansamycin antibiotics bind connected via a linker are effective for inducing the degrdn. and/or inhibition of HER-family tyrosine kinases. For example, a compd. of two geldanamycin moieties joined by a four-carbon linker provides selective degrdn. of HER-family tyrosine kinases, without substantially affecting other kinases. These compds. can be used for treatment of HER-pos. cancers with reduced toxicity, since these compds. potently kill cancer cells but affect fewer proteins than geldanamycin. Compd. prepn. is descibed.

IT **280145-12-2P 280145-13-3P 280145-14-4P**
280145-15-5P 301643-24-3P 301643-25-4P
301643-26-5P 301643-27-6P 301643-28-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(bifunctional hsp-binding deriv. for degrdn. and/or inhibition of HER-family tyrosine kinase and cancer treatment)

RN 280145-12-2 CAPLUS
CN Geldanamycin, 17,17'-(1,4-butanediyldiimino)bis[17-demethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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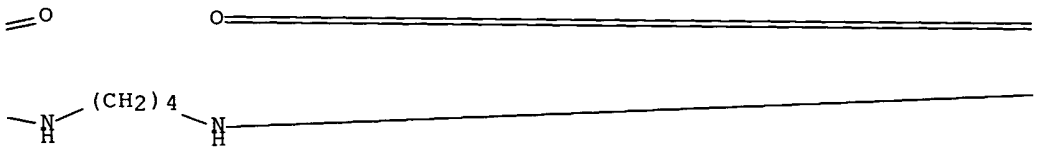

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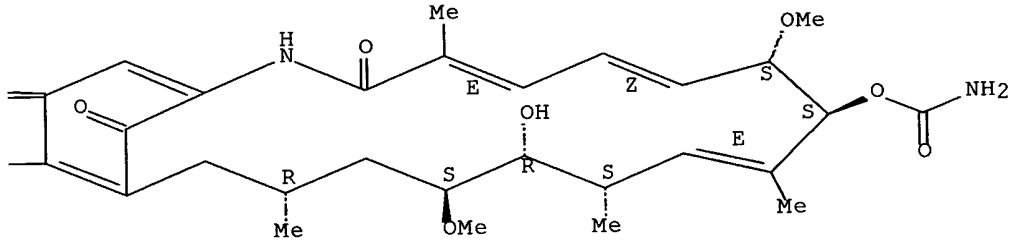
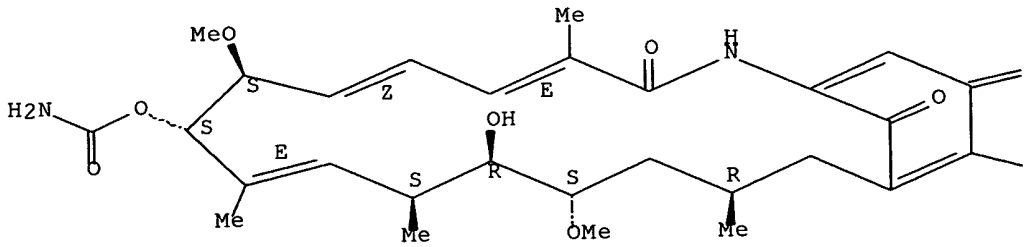


RN 280145-13-3 CAPLUS
CN Geldanamycin, 17,17'-(1,7-heptanediyldiimino)bis[17-demethoxy- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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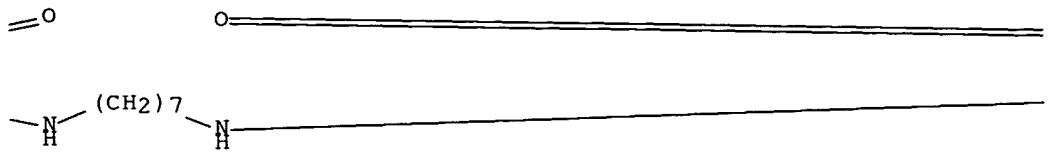

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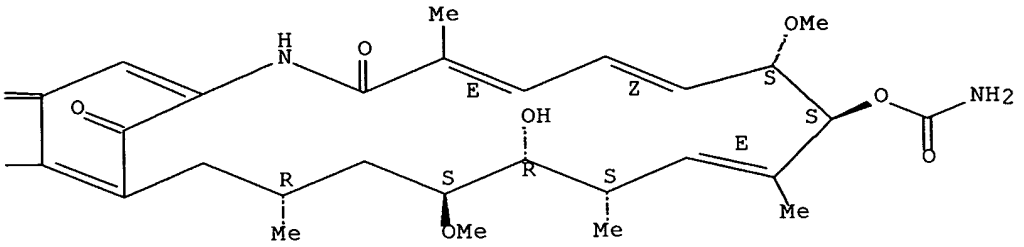

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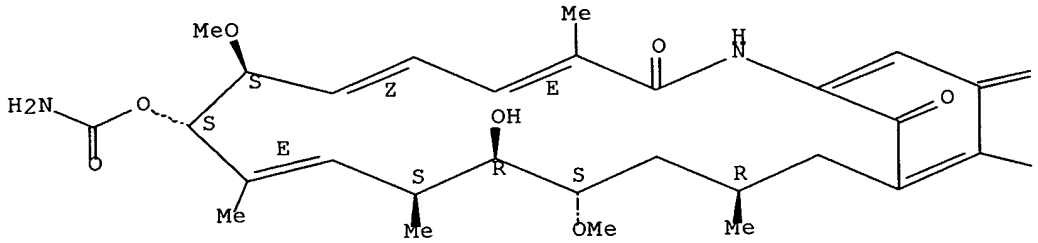
CN Geldanamycin, 17,17'-(1,9-nonanediyldiimino)bis[17-demethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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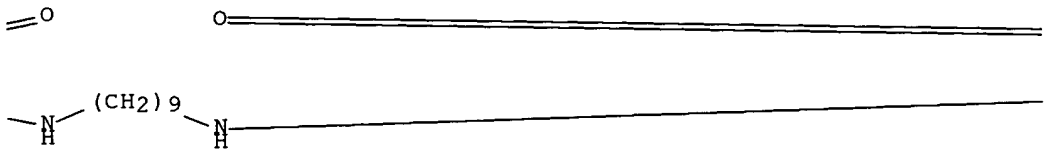

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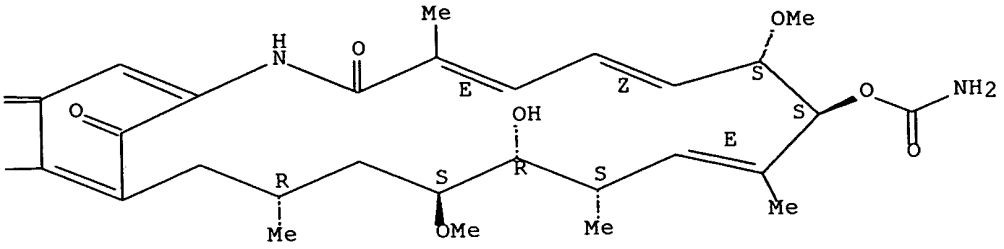
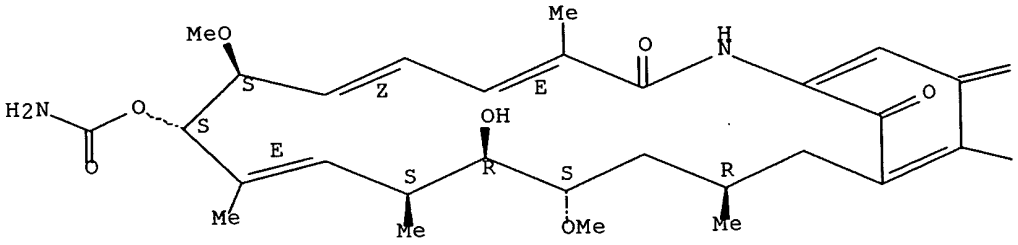


RN 280145-15-5 CAPLUS
CN Geldanamycin, 17,17'-(1,11-undecanediyldiimino)bis[17-demethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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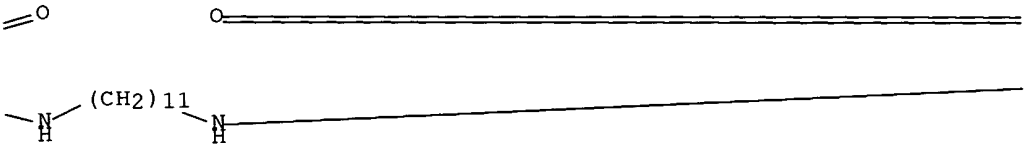

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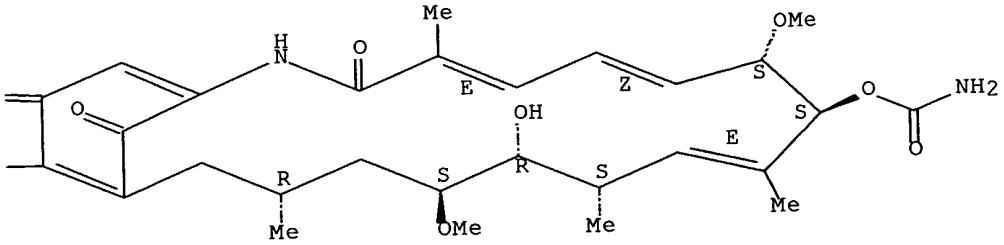
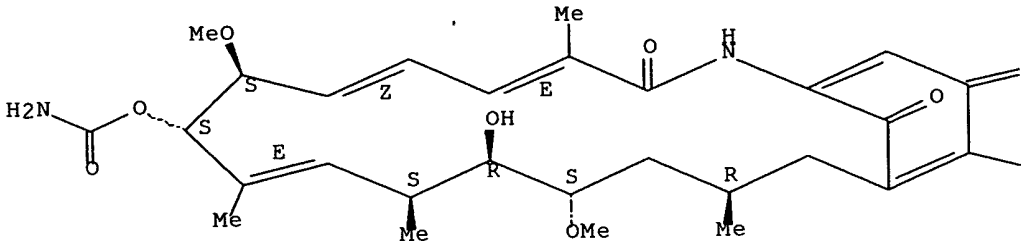


RN 301643-24-3 CAPLUS
CN Geldanamycin, 17,17'-(1,12-dodecanediyldiimino)bis[17-demethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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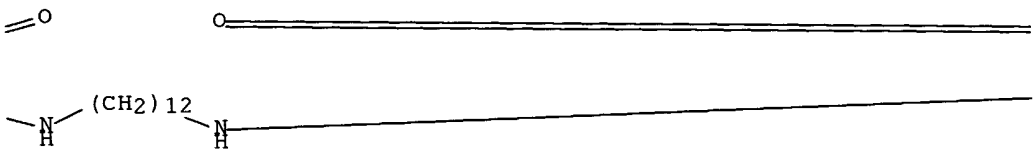

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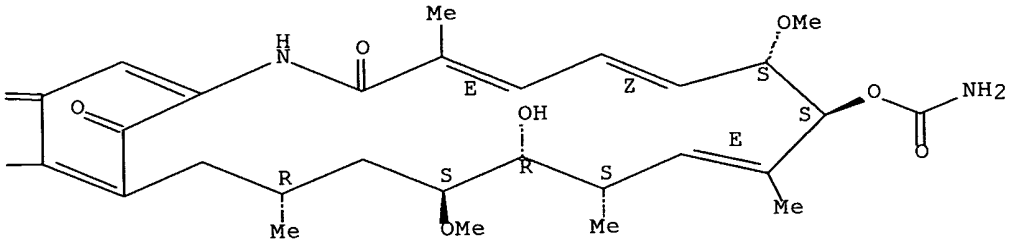
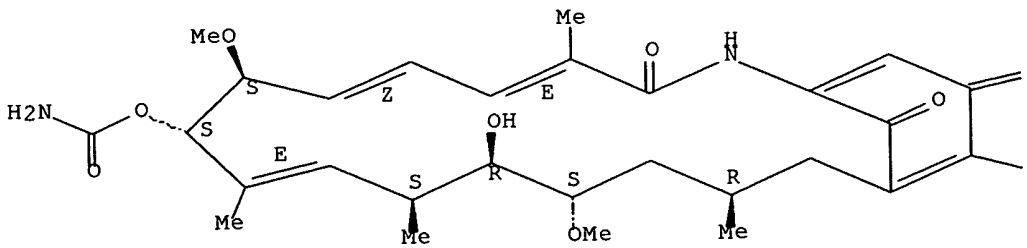


RN 301643-25-4 CAPLUS
CN Geldanamycin, 17,17'-(1,5-pentanediyldiimino)bis[17-demethoxy- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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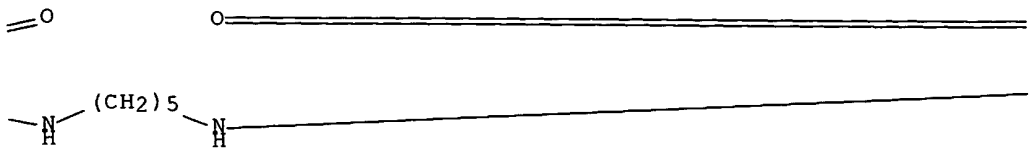

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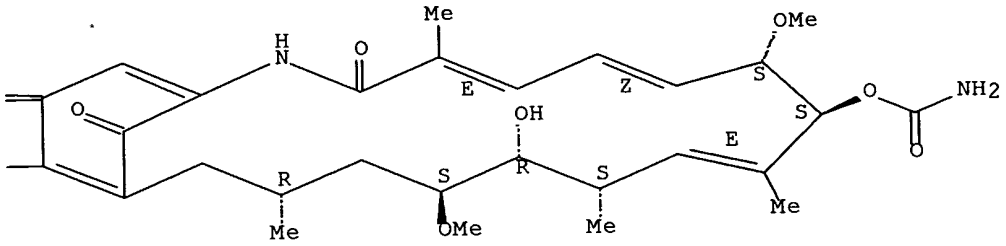
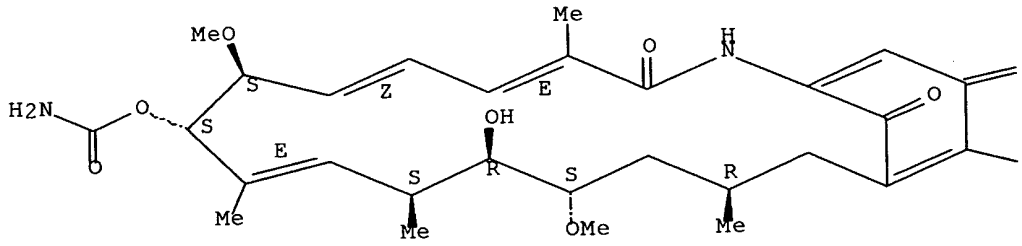


RN 301643-26-5 CAPLUS
CN Geldanamycin, 17,17'-(1,6-hexanediyldiimino)bis[17-demethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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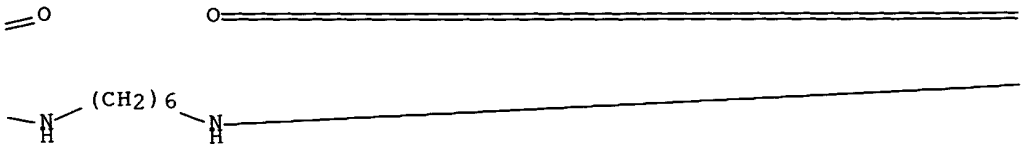

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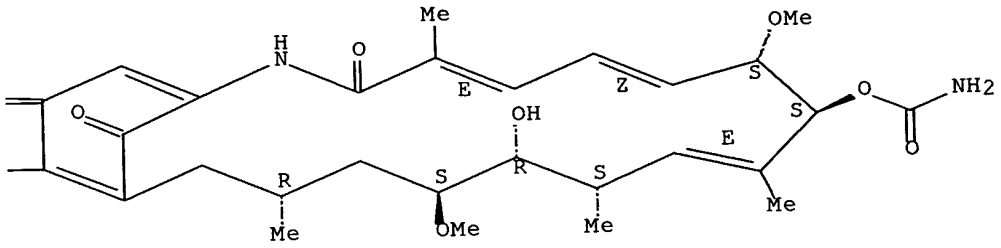
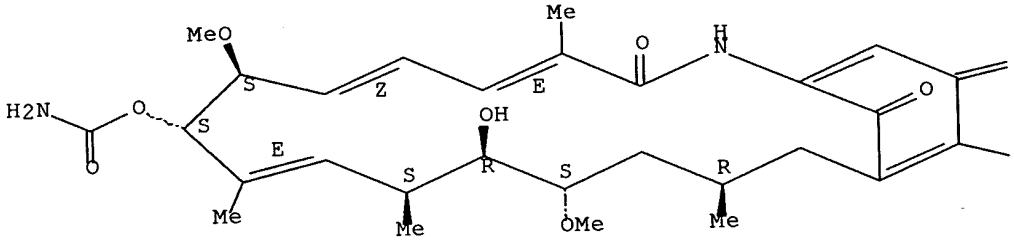


RN 301643-27-6 CAPLUS
CN Geldanamycin, 17,17'-(1,8-octanediyldiimino)bis[17-demethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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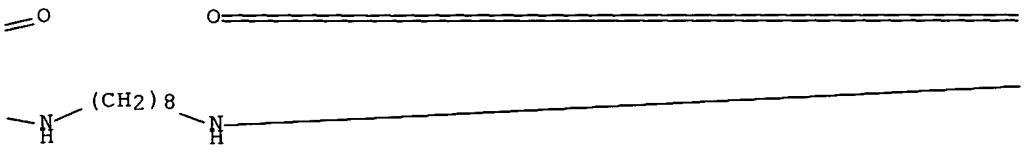

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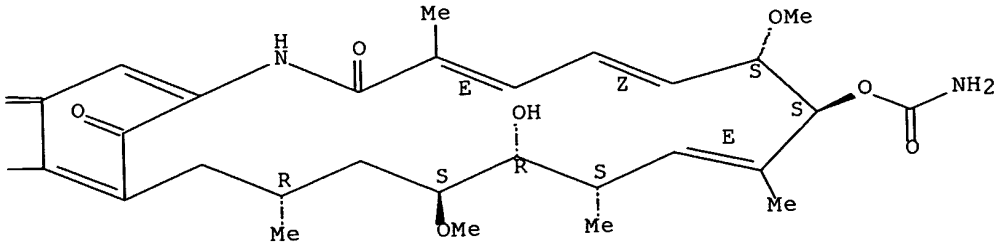
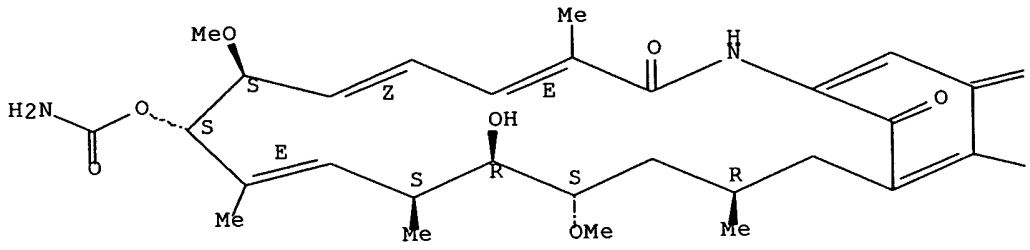


RN 301643-28-7 CAPLUS
CN Geldanamycin, 17,17'-(1,10-decanediyldiimino)bis[17-demethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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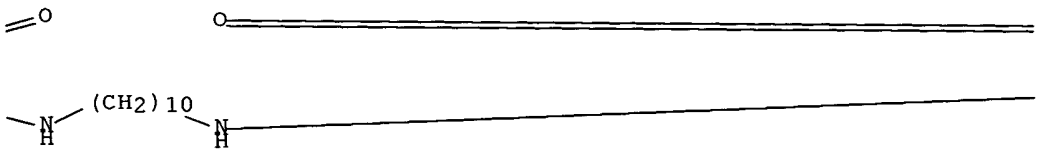

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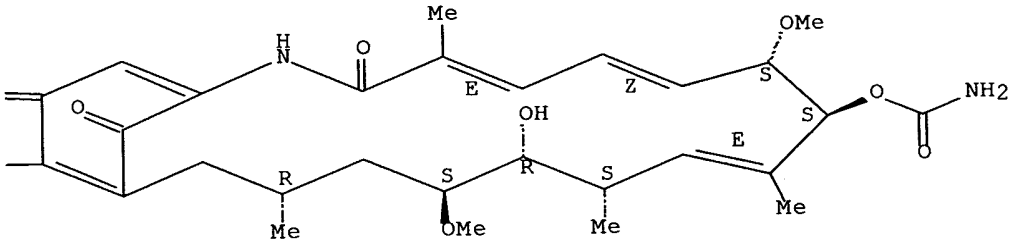
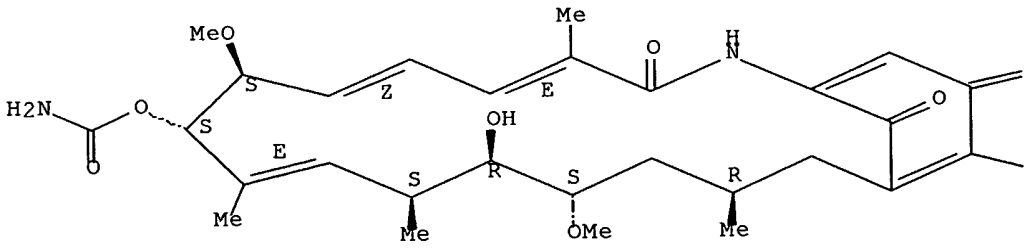


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2000:282715 CAPLUS
DN 133:83981
TI Identification of a geldanamycin dimer that induces the selective degradation of HER-family tyrosine kinases
AU Zheng, Fuzhong F.; Kuduk, Scott D.; Chiosis, Gabriela; Munster, Pamela N.; Sepp-Lorenzino, Laura; Danishefsky, Samuel J.; Rosen, Neal
CS Program in Cell Biology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SO Cancer Research (2000), 60(8), 2090-2094
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Geldanamycin (GM) is a natural antibiotic that binds Hsp90 and induces the degrdn. of receptor tyrosine kinases, steroid receptors, and Raf. It is a potent inhibitor of cancer cells that overexpress HER-kinases, but its effects on other important proteins may cause significant toxicity and limit its clin. use. The authors report the synthesis and identification of a GM dimer, GMD-4c, which had selective activity against HER-kinases. Selectivity was a function of linker length and required two intact GM moieties. GMD-4c is a potent inducer of G1 block and apoptosis of breast cancer cell lines that overexpress HER2, but does not appreciably inhibit the growth of 32D cells that lack HER-kinases. GMD-4c could be useful in the treatment of carcinomas dependent on HER-kinases.
IT **280145-12-2 280145-13-3 280145-14-4 280145-15-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification of a geldanamycin dimer that induces selective degrdn. of HER-family tyrosine kinases in relation to breast cancer inhibition)
RN 280145-12-2 CAPLUS
CN Geldanamycin, 17,17'-(1,4-butanediyldiimino)bis[17-demethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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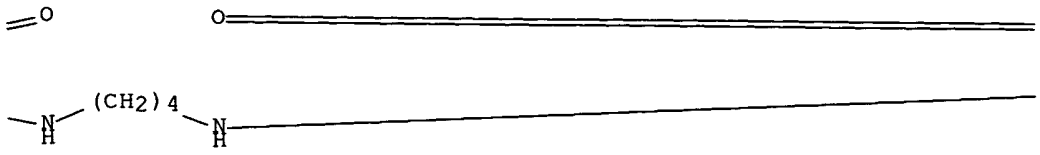

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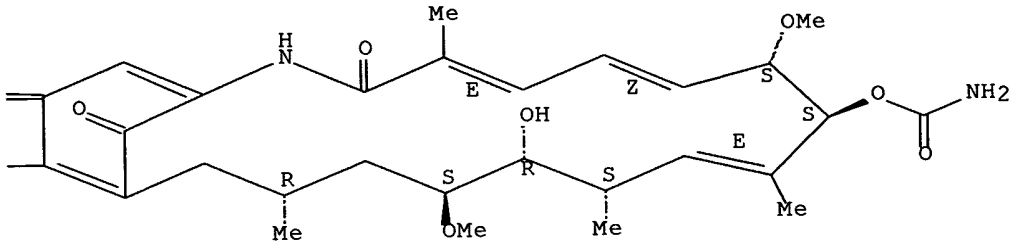

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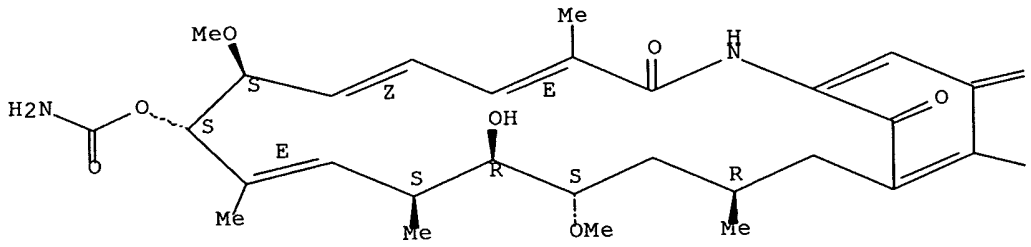
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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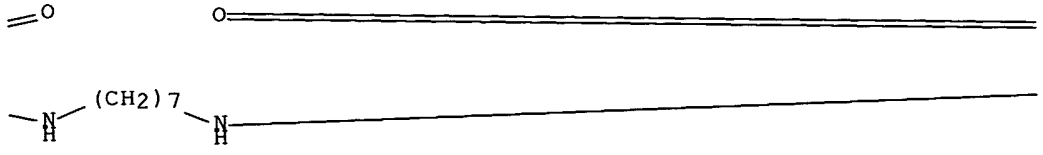

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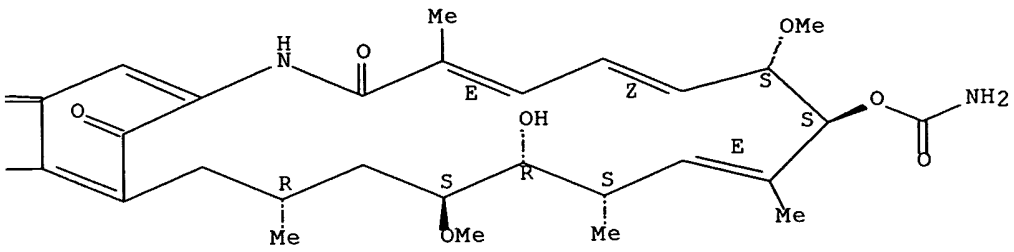

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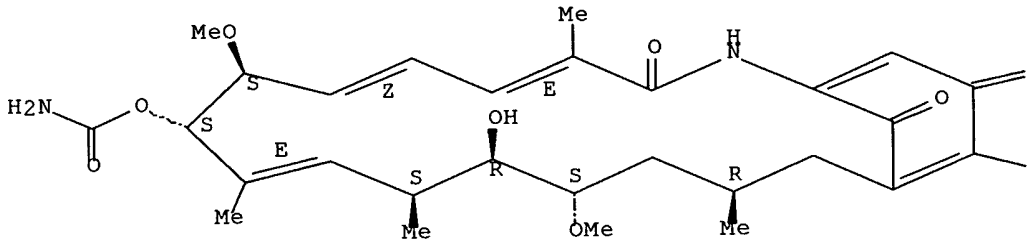
Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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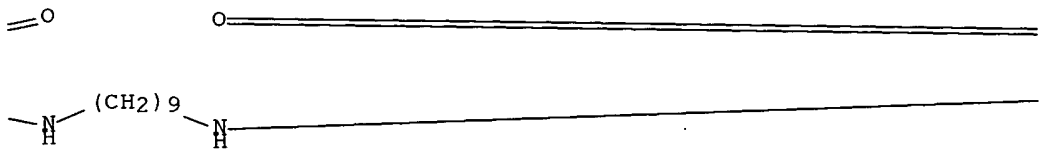

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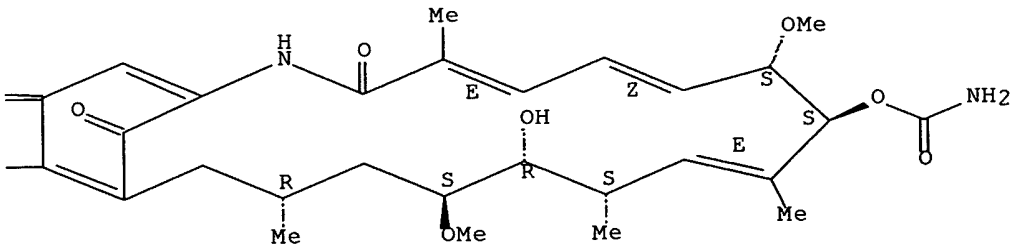

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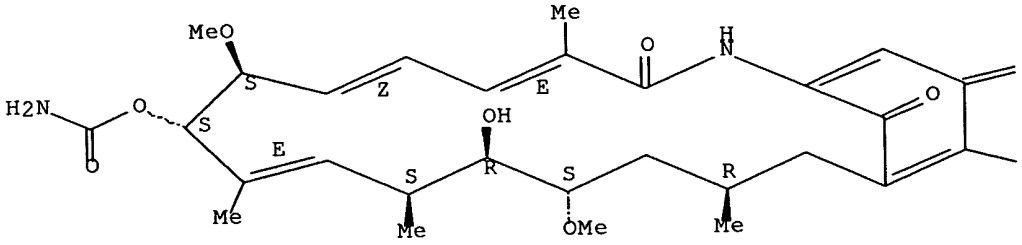
CN Geldanamycin, 17,17'-(1,11-undecanediyldiimino)bis[17-demethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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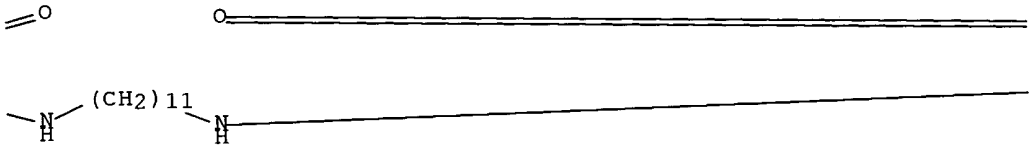

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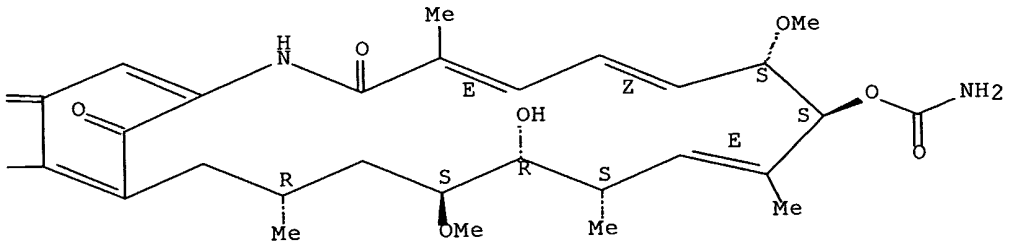

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

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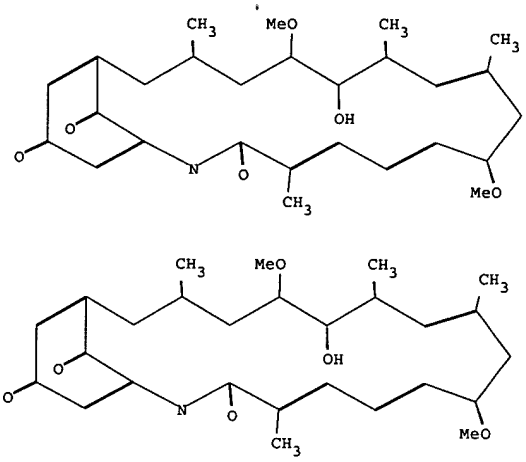
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